

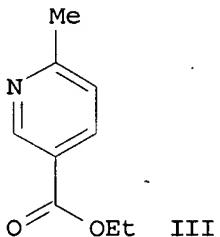
# STN-Structure Search

1/18/08

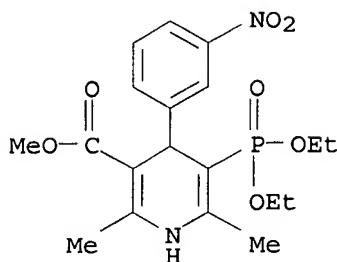
10/549,510

=> d ibib abs hitstr 1-26

L4 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2007:556242 CAPLUS  
 DOCUMENT NUMBER: 147:166161  
 TITLE: Regioselective synthesis of pyridines and dihydropyridines derived from  $\beta$ -amino acids and aminophosphonates by reaction of N-vinylic phosphazenes with  $\alpha,\beta$ -unsaturated ketones  
 AUTHOR(S): Palacios, Francisco; Herran, Esther; Rubiales, Gloria; Alonso, Concepcion  
 CORPORATE SOURCE: Departamento de Quimica Organica I, Facultad de Farmacia, Universidad del Pais Vasco, Vitoria, 01080, Spain  
 SOURCE: Tetrahedron (2007), 63(25), 5669-5676  
 CODEN: TETRAB; ISSN: 0040-4020  
 PUBLISHER: Elsevier Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 147:166161  
 GI



AB Reaction of N-vinylic phosphazenes, e.g. I, with  $\alpha,\beta$ -unsatd. ketones, e.g. II, leads to the formation of pyridines derived from  $\beta$ -amino acids, e.g. III, in a regioselective fashion. The use of functionalized enones derived from  $\alpha$ -acylstyryl-carboxylates or -phosphonates affords biol. active asym. and sym. dihydropyridines substituted with carboxylate or phosphonate groups including nitrendipine, felodipine, MRS 1097, and efonidipine analogs.  
 IT 98399-10-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of pyridine and dihydropyridine derived from  $\beta$ -amino acids and aminophosphonates via regioselective heterocyclization of vinylic phosphazenes with  $\alpha,\beta$ -unsatd. ketones)  
 RN 98399-10-1 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



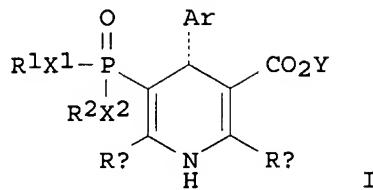
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

*On file 2*

L4 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:857416 CAPLUS  
 DOCUMENT NUMBER: 141:343535  
 TITLE: T-type calcium channel blockers  
 INVENTOR(S): Masuda, Yukinori; Furukawa, Taiji  
 PATENT ASSIGNEE(S): Nissan Chemical Industries Ltd., Japan  
 SOURCE: PCT Int. Appl., 39 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087172	A1	20041014	WO 2004-JP4432	20040329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004226547	A1	20041014	AU 2004-226547	20040329
CA 2520628	A1	20041014	CA 2004-2520628	20040329
EP 1609504	A1	20051228	EP 2004-724154	20040329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1764462	A	20060426	CN 2004-80008085	20040329
US 2007010490	A1	20070111	US 2005-549510	20050920
IN 2005DN04249	A	20070831	IN 2005-DN4249	20050920
NO 2005005015	A	20051115	NO 2005-5015	20051027
PRIORITY APPLN. INFO.:			JP 2003-90916	A 20030328
			JP 2003-393893	A 20031125
			WO 2004-JP4432	W 20040329

OTHER SOURCE(S): MARPAT 141:343535  
 GI



AB T-Type calcium channel blockers consisting of optically active 1,4-dihydropyridines represented by the general formula (I), pharmaceutically acceptable salts thereof, or solvates of both: I wherein R1 and R2 are each independently C1-6 alkyl, or R1 and R2 are united to form -CR5R6-CR7R8-, -CR5R6-CR7R8-CR9R10-, -CR5R6-CR7R8-CR9R10-CR11R12-, or the like; X1 and X2 are each independently O or NR13; Ar is optionally substituted Ph or the like; Ra and Rb are each independently C1-6 alkyl, -L2-NR16R17, CH2O-L2-NR16R17, CN, -L2-N(CH2CH2)2NR16, NR16R17, or the like; Y is C1-20 alkyl, -L3-NR18R19, (2) (3) (4) (5) or (6) and \* represents R-configuration.

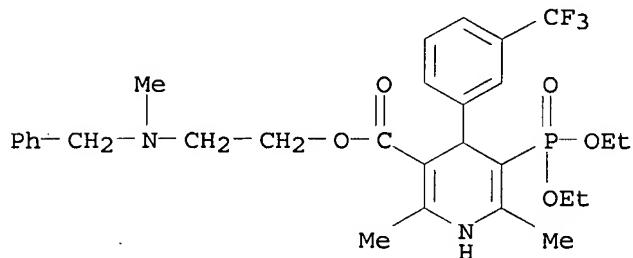
IT 98371-13-2 774235-87-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(1,4-dihydropyridines as T-type calcium channel blockers for treatment of related diseases)

RN 98371-13-2 CAPLUS

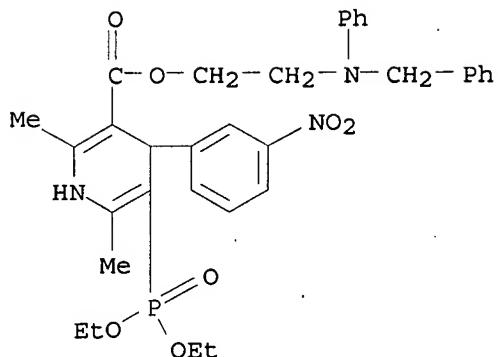
CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[3-(trifluoromethyl)phenyl]-, 2-[methyl(phenylmethyl)amino]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 774235-87-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[phenyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 . ANSWER 3 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:436962 CAPLUS

DOCUMENT NUMBER: 133:275838

TITLE: In search of selective P2 receptor ligands: interaction of dihydropyridine derivatives at recombinant rat P2X2 receptors

AUTHOR(S): Jacobson, K. A.; Kim, Y.-C.; King, B. F.

CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, Molecular Recognition Section, NIH, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892-0810, USA

SOURCE: Journal of the Autonomic Nervous System (2000), 81(1-3), 152-157

CODEN: JASYDS; ISSN: 0165-1838

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1,4-Dihydropyridines are regarded as privileged structures for drug design, i.e. they tend to bind to a wide variety of receptor sites. We have shown that upon appropriate manipulation of the substituent groups on a 1,4-dihydropyridine template, high affinity and selectivity for the A3 subtype of adenosine receptors ('P1 receptors') may be attained. In the present study we have begun to extend this approach to P2 receptors which are activated by ATP and other nucleotides. Nicardipine, a representative dihydropyridine, used otherwise as an L-type calcium channel blocker, was shown to be an antagonist at recombinant rat P2X2 ( $IC_{50}=25 \mu M$ ) and P2X4 ( $IC_{50} \text{ apprx. } 220 \mu M$ ) receptors expressed in *Xenopus* oocytes. Thus, this class of compds. represents a suitable lead for enhancement of affinity through chemical synthesis. In an attempt to modify the 1,4-dihydropyridine structure with a predicted P2 receptor recognition moiety, we have replaced one of the ester groups with a neg. charged phosphonate group. Several 4-phenyl-5-phosphonato-1,4-dihydropyridine derivs., MRS 2154 (2,6-dimethyl), MRS 2155 (6-methyl-2-phenyl), and MRS 2156 (2-methyl-6-phenyl), were synthesized through three component condensation reactions. These derivs. were not pure antagonists of the effects of ATP at P2X2 receptors, rather were either inactive (MRS 2156) or potentiated the effects of ATP in a concentration-dependent manner (MRS 2154 in the 0.3-10  $\mu M$  range and MRS 2155 at  $\text{1 } \mu M$ ). Antagonism of the effects of ATP at P2X2 receptor superimposed on the potentiation was also observed at  $\text{10 } \mu M$  (MRS 2154) or  $0.3-1 \mu M$  (MRS 2155). Thus, while a conventional dihydropyridine, nicardipine, was found to antagonize rat P2X2 receptors ninefold more potently than P2X4 receptors, the effects of novel, anionic 5-phosphonate analogs at the receptor were more complex.

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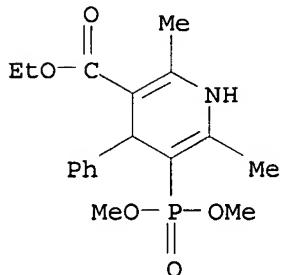
IT 300344-20-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of dihydropyridine derivs. and interaction at recombinant rat P2X2 receptors)

RN 300344-20-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-phenyl-, ethyl ester (CA INDEX NAME)



REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:487576 CAPLUS

DOCUMENT NUMBER: 129:216495

TITLE: (Coumarinyl)-1,4-dihydropyridine derivatives

AUTHOR(S): Valenti, P.; Rampa, A.; Budriesi, R.; Bisi, A.; Chiarini, A.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy

SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(6), 803-810

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 1,4-dihydropyridines bearing a coumarin moiety in 4-position was synthesized. The compds. were evaluated for inotropic, chronotropic and calcium antagonist activities. The replacement of the o-nitrophenyl moiety of nifedipine with a coumarin or phenylcoumarin system is accompanied by a decrease of the activity on myocardial and vascular parameters, but the synthesized compds. showed selective inhibiting effects on cardiac contractility and frequency.

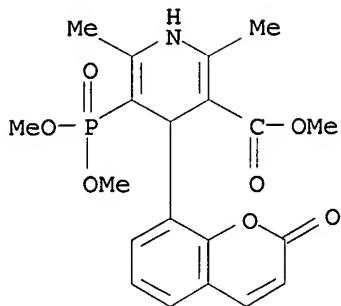
IT 212516-06-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and inotropic, chronotropic and calcium antagonistic activity of (coumarinyl)dihydropyridine derivs.)

RN 212516-06-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(2-oxo-2H-1-benzopyran-8-yl)-, methyl ester (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:272234 CAPLUS

DOCUMENT NUMBER: 128:321541

TITLE: Novel Hantzsch 1,4-dihydropyridines to study the structure-function relationships of calcium channels and photoinduced relaxation

AUTHOR(S): Iqbal, Nadeem; Triggle, Christopher R.; Knaus, Edward E.

CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, T6G 2N8, Can.

SOURCE: Drug Development Research (1997), 42(3/4), 120-130

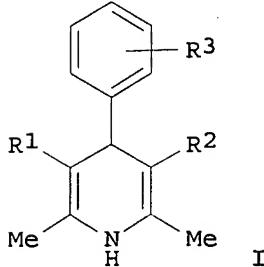
CODEN: DDREDK; ISSN: 0272-4391

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB A group of Me 1,4-dihydro-2,6-dimethyl-4-(2-, 3- or 4-NHOH; 3- or 4-N:O)-phenyl-5-pyridinecarboxylates possessing a C-3 CO<sub>2</sub>Me or NO<sub>2</sub> substituent, I (R1 = CO<sub>2</sub>Me, R2 = CO<sub>2</sub>Me, NO<sub>2</sub>, R3 = 2-, 3-, 4-NHOH, 3-, 4-N:O), were synthesized by reduction of the C-4 nitrophenyl precursors to the corresponding phenylhydroxylamine derivs. using 5% rhodium-on-charcoal with hydrazine hydrate as the hydrogen donor, followed by re-oxidation of the phenylhydroxylamine product to the corresponding nitrosophenyl derivative using pyridinium chlorochromate. A series of 1,4-dihydro-2,6-dimethyl-4-[(2-trifluoromethyl)phenyl]pyridines I [R1 = CO<sub>2</sub>Me, cyano, NO<sub>2</sub>, R2 = CO<sub>2</sub>Me, COMe, P(O)OEt<sub>2</sub>, CONH<sub>2</sub>, NH<sub>2</sub>, R3 = 2-CF<sub>3</sub>, 2-NO<sub>2</sub>], possessing CO<sub>2</sub>Me, COMe, CONH<sub>2</sub>, P(O)OEt<sub>2</sub>, CN, NO<sub>2</sub> C-3/C-5 substituents, were synthesized using a modified Hantzsch reaction involving the condensation of 2-(trifluoromethyl)benzaldehyde with an aminocrotonate and a ketone derivative. In vitro calcium channel (CC) activities were determined using a muscarinic-receptor-mediated Ca<sup>2+</sup>-dependent contraction of guinea pig

ileal longitudinal smooth muscle assay. This class of compds. exhibited weak CC antagonist activity [10<sup>-4</sup> to 10<sup>-7</sup> M range] relative to the reference drug nifedipine [IC<sub>50</sub> = 1.4 + 10<sup>-8</sup> M]. Structure-activity relationships [SARs] acquired were in agreement with known SARs where the relative potency order for C-4 Ph substituents is ortho and meta > para. A C-3 nitro substituent decreased CC antagonist activity. Compds. I possessing C-3 cyano or NO<sub>2</sub>, and a C-5 CO<sub>2</sub>Me, NO<sub>2</sub>, CONH<sub>2</sub>, COMe, or P(=O)OEt<sub>2</sub>, substituents exhibited weak CC antagonist activity in the 10<sup>-4</sup> to 10<sup>-5</sup> M range. Although this group of highly functionalized 1,4-dihydropyridines are not useful CC antagonists, they will serve as valuable model compds. to study the structure-function relationships of CC modulation.

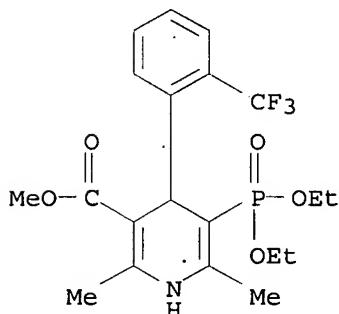
IT 98399-11-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation, calcium channel antagonistic activity, and structure activity of Hantzsch pyridines)

RN 98399-11-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[2-(trifluoromethyl)phenyl]-, methyl ester (CA INDEX NAME)



REFERENCE COUNT:

43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:226525 CAPLUS

DOCUMENT NUMBER: 128:282763

TITLE: Design and synthesis of haptens for application to the preparation of chiral 1,4-dihydropyridines

AUTHOR(S): Ikeda, Kiyoshi; Kato, Tatsuhisa; Suzuki, Takehisa; Achiwa, Kazuo

CORPORATE SOURCE: School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, 422, Japan

SOURCE: Chemical &amp; Pharmaceutical Bulletin (1998), 46(3), 518-522

PUBLISHER: CODEN: CPBTAL; ISSN: 0009-2363

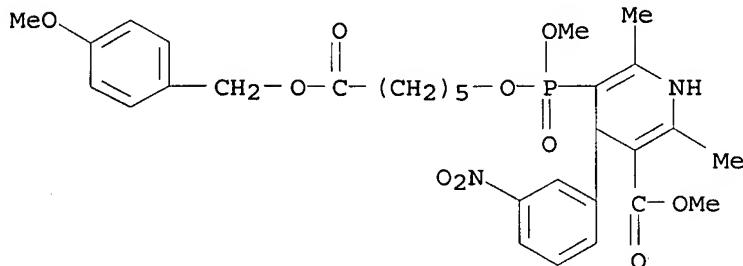
DOCUMENT TYPE: Pharmaceutical Society of Japan

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:282763

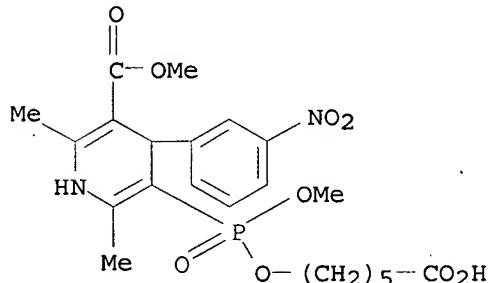
AB Lipase-catalyzed enzymic hydrolysis of di-Me esters of 1,4-dihydropyridines to the monoester, which is an important intermediate for the synthesis of optically active 1,4-dihydropyridines, does not proceed directly. The design and synthesis of novel haptens having a phosphonate group containing the requisite oxyanionic character to mimic the tetrahedral intermediate of hydrolysis, and the application of these compds. for generating antibodies with catalytic ability for the enantioselective partial hydrolysis of 1,4-dihydro-2,6-dimethyl-4-(3-

CN 3-Pyridinecarboxylic acid, 1,4-dihydro-5-[methoxy[[6-[(4-methoxyphenyl)methoxy]-6-oxohexyl]oxy]phosphinyl]-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



RN 205752-56-3 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[(5-carboxypentyl)oxy]methoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 3-methyl ester (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:320271 CAPLUS

DOCUMENT NUMBER: 125:48354

TITLE: Structure-activity relationship studies of xanthone and fluorenone-1,4-dihydropyridine-5-phosphonates

AUTHOR(S): Budriesi, Roberta; Rampa, Angela; Bisi, Alessandra; Fabbri, Giuseppina; Chiarini, Alberto; Valenti, Piero

CORPORATE SOURCE: Dep. Pharmaceutical Sci., Univ. Bologna, Italy

SOURCE: Arzneimittel-Forschung (1996), 46(4), 374-377

CODEN: ARZNAD; ISSN: 0004-4172

PUBLISHER: Cantor

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of xanthone and fluorenone-1,4-dihydropyridine derivs. bearing a 5-phosphonate group were prepared. The compds. were evaluated for inotropic, chronotropic and calcium antagonistic properties. The insertion of a phosphonate group is detrimental for inotropic and calcium antagonist activity but improves the potency and selectivity for chronotropism.

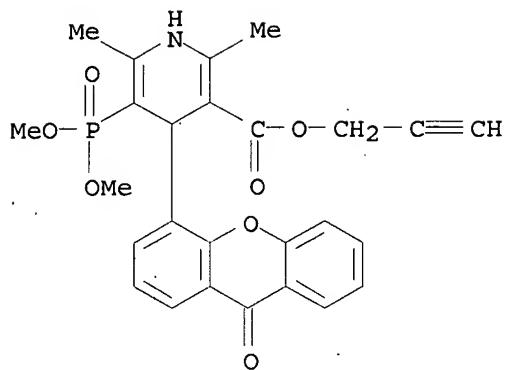
IT 178113-17-2P 178113-18-3P 178113-19-4P

178113-20-7P 178113-21-8P 178113-27-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

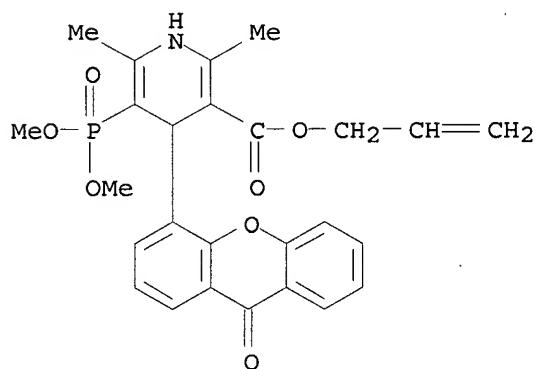
(preparation and structure-activity relationship studies of xanthone- and fluorenone-dihydropyridine phosphonates)

RN 178113-17-2 CAPLUS



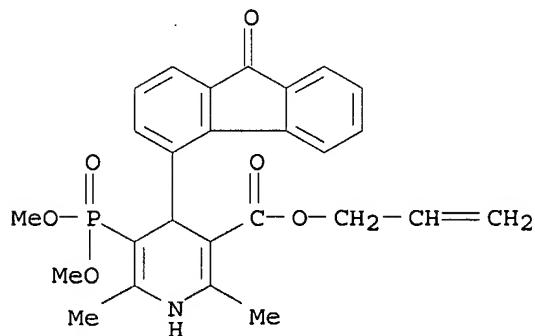
RN 178113-21-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(9-oxo-9H-xanthen-4-yl)-, 2-propenyl ester (9CI) (CA INDEX NAME)



RN 178113-27-4 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(9-oxo-9H-fluoren-4-yl)-, 2-propenyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:30121 CAPLUS

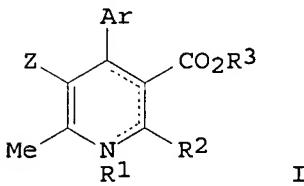
DOCUMENT NUMBER: 114:30121

TITLE: Drug effect-enhancing agent for antitumor drug

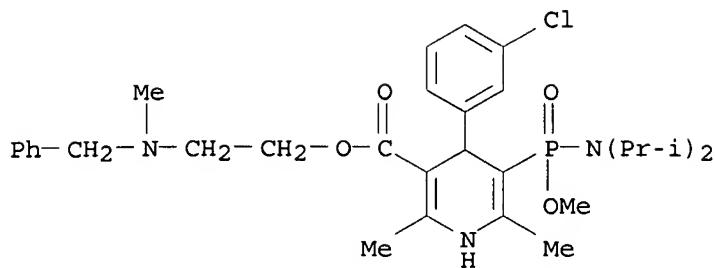
INVENTOR(S): Akiyama, Shinichi; Sakoda, Ryozo; Seto, Kiyotomo;  
 Shudo, Norimasa  
 PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan  
 SOURCE: Eur. Pat. Appl., 40 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 353692	A2	19900207	EP 1989-114113	19890731
EP 353692	A3	19910508		
EP 353692	B1	19951004		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE JP 02138221	A	19900528	JP 1989-168549	19890630
JP 2850376	B2	19990127		
CA 1334752	C	19950314	CA 1989-607026	19890731
EP 655455	A1	19950531	EP 1995-101310	19890731
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE AT 128623	T	19951015	AT 1989-114113	19890731
US 5130303	A	19920714	US 1991-729904	19910715
US 5304550	A	19940419	US 1993-57902	19930507
US 5508403	A	19960416	US 1995-463511	19950605
PRIORITY APPLN. INFO.:			JP 1988-193002	A 19880802
			JP 1989-168549	A 19890630
			US 1989-386254	B1 19890728
			EP 1989-114113	A3 19890731
			US 1991-729904	A3 19910715
			US 1992-865489	A3 19920409

OTHER SOURCE(S): CASREACT 114:30121; MARPAT 114:30121  
 GI

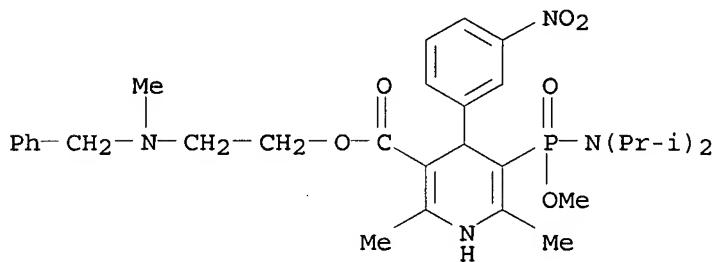


AB Pyridine derivs. I [Ar = (un)substituted Ph, pyridyl, furyl, 2,1,3-benzoxadiazol-4-yl; R1 = C1-4 alkyl, CH2Ph, substituted alkylene; R2 = C1-4 alkyl, CHO, CN, CH2OH, NH2, etc.; R3 = H, C1-12 alkyl, C3-6 alkenyl or cycloalkyl, aminoalkyl, benzylpiperidinyl, etc.; Z = P(O)R4R5, CO2R3; R4, R5 = OH, C1-12 alkoxy, aryloxy, etc., or R4R5 = OYO, NHYO, NHYNH, etc.; Y = (substituted) C2-4 alkylene] enhance the effects of antitumor drugs on cancer cells and suppress the drug resistance of the cancer cells. Thus, taking the resistance of KB-3-1 human carcinoma cells to vincristine as 1, the relative resistance of the multidrug-resistant KB-C1 variant of KB-3-1 cells was 1200, and the relative resistance of KB-3-1 and KB-C1 cells to vincristine in the presence of 10  $\mu$ g I [1,4-dihydropyridine ring, Ar = m-nitrophenyl, R1 = H, R2 = Me, R3 = 2-(4-diphenylmethyl-1-piperazinyl)ethyl, Z = P(O)R4R5, R4R5 = OCHMeCH2CHMeO] (II) was 0.1 and 1.0, resp. A mixture of II-HCl 30, adriamycin 7.5, and Macrogol 400 130 g was combined with a coating solution of gelatin 93, glycerol 19, D-sorbitol 10, Et p-hydroxybenzoate 0.4, Pr



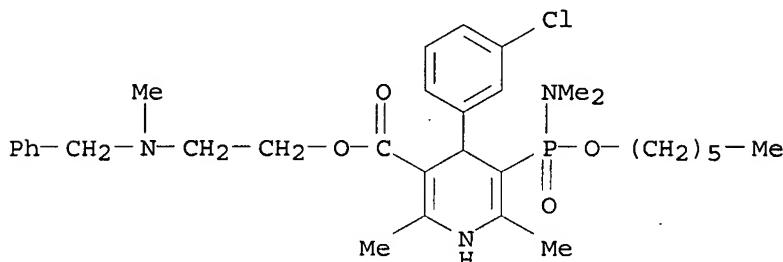
RN 131332-67-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[(bis(1-methylethyl)amino)methoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



RN 131332-75-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 4-(3-chlorophenyl)-5-[(dimethylamino)(hexyloxy)phosphinyl]-1,4-dihydro-2,6-dimethyl-2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



L4 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1990:544853 CAPLUS

DOCUMENT NUMBER: 113:144853

TITLE: Two pyridine analogs with more effective ability to reverse multidrug resistance and with lower calcium channel blocking activity than their dihydropyridine counterparts

AUTHOR(S): Shudo, Norimasa; Mizoguchi, Tetsuro; Kiyosue, Tatsuto; Arita, Makoto; Yoshimura, Akihiko; Seto, Kiyotomo; Sakoda, Ryozo; Akiyama, Shinichi

CORPORATE SOURCE: Fac. Med., Kagoshima Univ., Kagoshima, 890, Japan  
SOURCE: Cancer Research (1990), 50(10), 3055-61DOCUMENT TYPE: CODEN: CNREA8; ISSN: 0008-5472  
Journal

LANGUAGE: English

AB Four pyridine analogs and their dihydropyridine counterparts were examined for their ability to reverse drug resistance in a multidrug-resistant human carcinoma cell line, KB-C2. Two pyridine analogs were more able to reverse drug resistance than their dihydropyridine counterparts. The other two pyridine analogs had an effect on drug resistance similar to their dihydropyridine counterparts. The calcium channel-blocking activity of all the pyridine analogs was considerably lower than that of the dihydropyridine analogs. Of the pyridine analogs, 2-[4-(diphenylmethyl)-1-piperazinyl]ethyl 5-(trans-4,6-dimethyl-1,3,2-dioxaphosphorinan-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-3-pyridinecarboxylate P-Oxide (PAK-104P) was the most effective in reversing multidrug resistance. PAK-104P (1 and 5  $\mu$ M) completely reversed the drug resistance in KB-8-5 and KB-C2 cells, resp. The reversing effect of PAK-104P was greater than that of other multidrug resistance-reversing agents, cepharamthine, verapamil, nimodipine, and nicardipine. PAK-104P at 1  $\mu$ M increased about 10-fold the accumulation of vinblastine in KB-C2 cells, whereas verapamil at the same concentration increased the accumulation about 2-fold. The inhibition of [<sup>3</sup>H]azidopine photolabeling of P-glycoprotein by the pyridine and dihydropyridine analogs except 2-[methyl(phenylmethyl)amino]ethyl 4-(2-chlorophenyl)-5-(4-methyl-1,3,2-dioxaphosphorinan-2-yl)-1,4-dihydro-2,6-dimethyl-3-pyridinecarboxylate P-Oxide correlated with the reversing of drug resistance by the analogs. Some newly synthesized pyridine analogs seemed to have lower calcium channel-blocking activity and more potent resistance-reversing ability than verapamil and other calcium channel blockers.

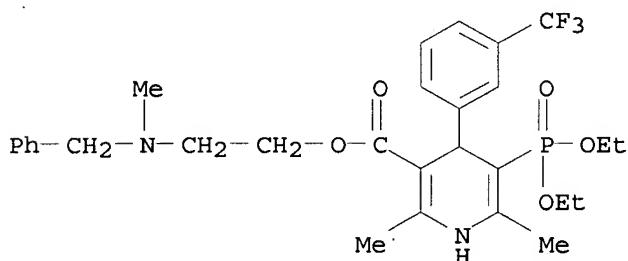
IT 98398-96-0

RL: BIOL (Biological study)

(multidrug resistance reversal by, in neoplasm cells of humans)

RN 98398-96-0 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[3-(trifluoromethyl)phenyl]-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



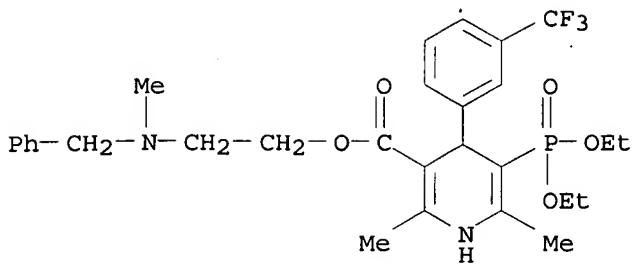
IT 98371-13-2P, PAK 101

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and multidrug resistance-reversing activity of, in human neoplasm cells)

RN 98371-13-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[3-(trifluoromethyl)phenyl]-, 2-[methyl(phenylmethyl)amino]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1990:434417 CAPLUS

DOCUMENT NUMBER: 113:34417

TITLE: Overcoming drug resistance in cancer cells with dihydropyridine analogs

AUTHOR(S): Kamiwatari, Mikio

CORPORATE SOURCE: Fac. Med., Kagoshima Univ., Kagoshima, 890, Japan

SOURCE: Kagoshima Daigaku Igaku Zasshi (1989), 41(3), 225-34

CODEN: KDIZAA; ISSN: 0368-5063

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Ten newly synthetic dihydropyridine (DHP) analogs were investigated for their ability to reverse drug resistance in a multidrug-resistant human carcinoma cell line, KB-Cl. The resistance was reversed completely by 4 DHP analogs, partially by 3, and little by 3. The radioactive photoactive DHP Ca<sup>2+</sup> channel blocker, [<sup>3</sup>H]azidopine (I) photolabeled P-glycoprotein (P-GP) in membrane vesicles from KB-Cl cells. This photolabeling was almost completely inhibited by excess DHP analogs that reversed or lowered drug resistance. In contrast, the labeling was not inhibited by analogs that did not reverse the resistance. Among other reversing agents, cepharanthine and reserpine inhibited the [<sup>3</sup>H]I photolabeling, but thioridazine did not. SDB-ethylenediamine slightly inhibited the labeling at 100  $\mu$ M. Vinblastine also inhibited the labeling. The correlation between the reversing of the drug resistance and the inhibition of [<sup>3</sup>H]I photolabelling of P-GP by DHP suggests a role for P-GP in multidrug-resistance and also the reversing of the resistance by DHP analogs.

IT 95242-45-8 95242-46-9 113979-05-8

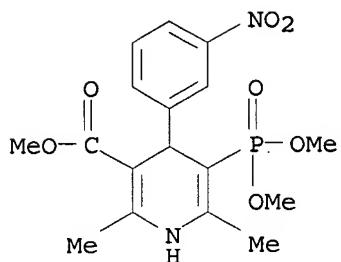
121912-21-8

RL: BIOL (Biological study)

(antitumor drug resistance inhibition by, P-glycoproteins in)

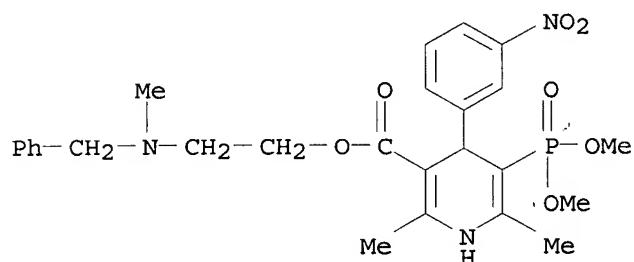
RN 95242-45-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



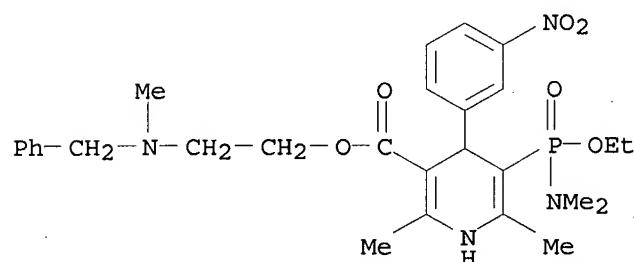
RN 95242-46-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



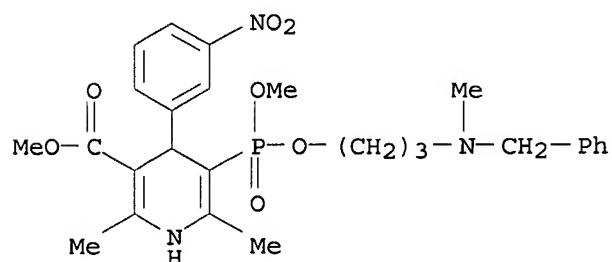
RN 113979-05-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[(dimethylamino)ethoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)

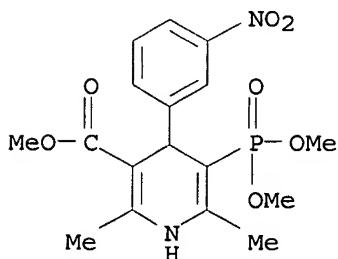


RN 121912-21-8 CAPLUS

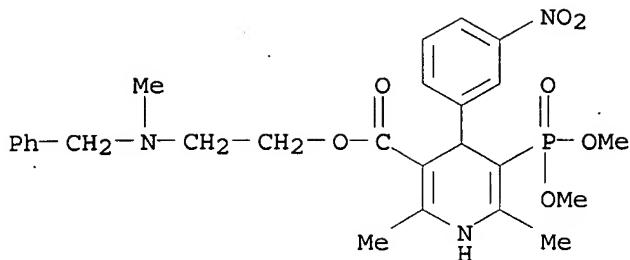
CN 3-Pyridinecarboxylic acid, 1,4-dihydro-5-[methoxy[3-[methyl(phenylmethyl)amino]propoxy]phosphinyl]-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



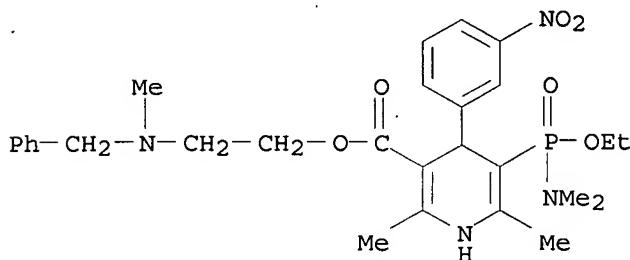
L4 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1989:470430 CAPLUS  
 DOCUMENT NUMBER: 111:70430  
 TITLE: Correlation between reversing of multidrug resistance and inhibiting of [<sup>3</sup>H]azidopine photolabeling of P-glycoprotein by newly synthesized dihydropyridine analogs in a human cell line  
 AUTHOR(S): Kamiwatari, Mikio; Nagata, Yukihiko; Kikuchi, Hiroshi; Yoshimura, Akihiko; Sumizawa, Tomoyuki; Shudo, Norimasa; Sakoda, Ryozo; Seto, Kiyotomo; Akiyama, Shinichi  
 CORPORATE SOURCE: Fac. Med., Kagoshima Univ., Kagoshima, 890, Japan  
 SOURCE: Cancer Research (1989), 49(12), 3190-5  
 CODEN: CNREA8; ISSN: 0008-5472  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Ten synthetic dihydropyridine analogs were investigated for their ability to reverse drug resistance in a multidrug-resistant human carcinoma cell line, KB-Cl. Four dihydropyridine analogs completely reversed the resistance, 3 lowered the resistance, and 3 had little effect. The radiolabeled photoactive dihydropyridine calcium channel blocker, [<sup>3</sup>H]azidopine, photolabels P-glycoprotein in membrane vesicles from KB-Cl cells. This photolabeling was almost completely inhibited by excess dihydropyridine analog that reversed or lowered drug resistance. In contrast, the labeling was not inhibited by analogs that do not reverse resistance. Among other reversing agents, cepharamthine and reserpine inhibited the [<sup>3</sup>H]azidopine photolabeling, but thioridazine did not. N-Solanesyl-N,N'-bis(3,4-dimethoxybenzyl)ethylenediamine slightly inhibited the labeling at 100  $\mu$ M. An anticancer agent, vinblastine, also inhibited the labeling. The correlation between the reversing of the drug resistance and the inhibition of the [<sup>3</sup>H]azidopine photolabeling of P-glycoprotein by dihydropyridine analogs suggests a role for P-glycoprotein in multidrug resistance and also the reversing of the resistance by dihydropyridine analogs.  
 IT 95242-45-8, PAK 10 95242-46-9, PAK 6 113979-05-8  
 , PAK 1 121912-21-8, PAK 7  
 RL: BIOL (Biological study)  
 (neoplasm multidrug resistance-reversing activity of, calcium channel blockade and P glycoprotein in relation to, in human cells)  
 RN 95242-45-8 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



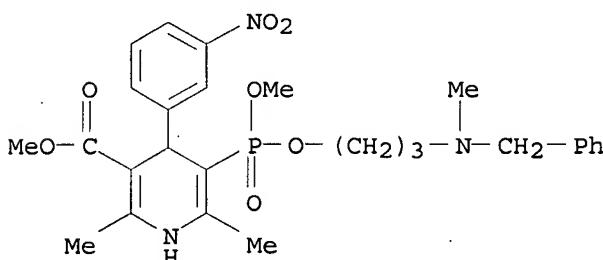
RN 95242-46-9 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



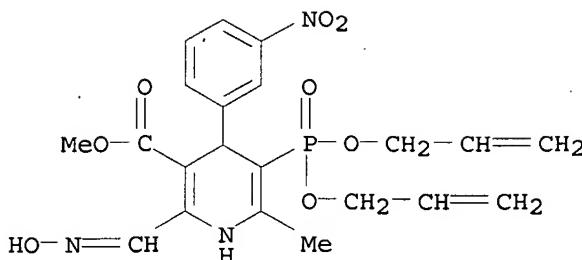
RN 113979-05-8 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-[(dimethylamino)ethoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



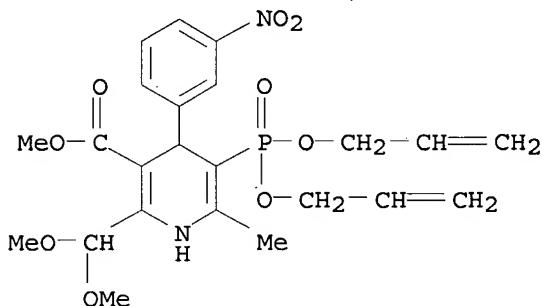
RN 121912-21-8 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 1,4-dihydro-5-[methoxy[3-[methyl(phenylmethyl)amino]propoxy]phosphinyl]-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



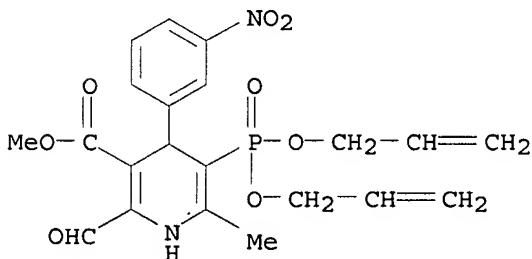
L4 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1989:23995 CAPLUS  
 DOCUMENT NUMBER: 110:23995  
 TITLE: Syntheses and antihypertensive activities of  
       1,4-dihydropyridine-5-phosphonate derivatives. III  
       Morita, Iwao; Haruta, Yuko; Tomita, Toshio; Tsuda,  
       Masami; Kandori, Kazuhisa; Kise, Masahiro; Kimura,  
       Kiyoshi  
 AUTHOR(S):  
 CORPORATE SOURCE: Res. Lab., Nippon Shinyaku Co., Ltd., Kyoto, 601,  
                   Japan  
 SOURCE: Chemical & Pharmaceutical Bulletin (1987), 35(12),  
           4819-28  
 DOCUMENT TYPE: CODEN: CPBTAL; ISSN: 0009-2363  
 LANGUAGE: Journal  
 OTHER SOURCE(S): English  
                   CASREACT 110:23995



IT 115550-24-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation, deprotection, and antihypertensive activity of)  
 RN 115550-24-8 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-[bis(2-propenyloxy)phosphinyl]-2-(dimethoxymethyl)-1,4-dihydro-6-methyl-4-(3-nitrophenyl)-, methyl ester  
 (9CI) (CA INDEX NAME)



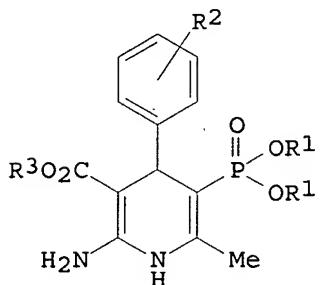
IT 115569-95-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation, reduction, and antihypertensive activity of)  
 RN 115569-95-4 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 5-[bis(2-propenyloxy)phosphinyl]-2-formyl-1,4-dihydro-6-methyl-4-(3-nitrophenyl)-, methyl ester (9CI) (CA INDEX NAME)



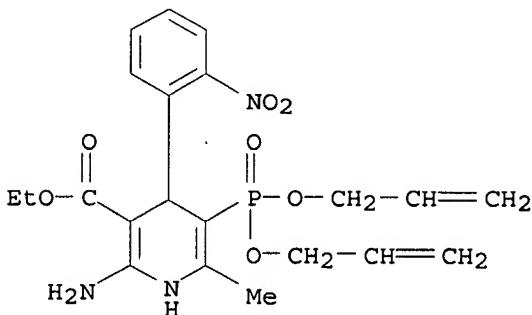
L4 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1988:570646 CAPLUS  
 DOCUMENT NUMBER: 109:170646  
 TITLE: Preparation of phosphorus-containing  
 2-amino-1,4-dihydropyridine derivatives as  
 calcium-antagonistic antihypertensives and  
 vasodilators  
 INVENTOR(S): Kimura, Kiyoshi; Kise, Masahiro; Morita, Iwao; Tsuda,

Masami  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

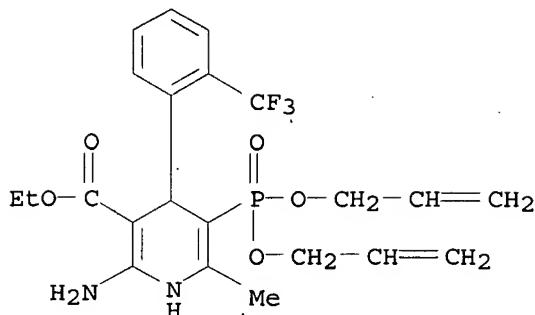
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63115889	A	19880520	JP 1986-261586	19861031
PRIORITY APPLN. INFO.:			JP 1986-261586	19861031
OTHER SOURCE(S):			CASREACT 109:170646; MARPAT 109:170646	
GI				



AB The title derivs. I [R1 = alkenyl; R1R1 = (CH2)3; R2 = NO2, CF3, halo; R3 = lower alkyl] and their pharmacol. acceptable salts are prepared EtOH solution of EtONa was added to EtOH solution of 2-[1-(2-nitrobenzylidene)acetyl]-2-oxo-1,3,2-dioxaphosphorinane (1.55 g) and H2NC(:NH)CH2CO2Et.HCl (0.833 g) under stirring at 0° and the reaction mixture was refluxed for 6 h to give 0.92 g I [R1R1 = (CH2)3, R2 = 2-NO2, R3 = Et] which was tested for spontaneously hypertensive rats to show ED30 of 0.9 mg/kg p.o., vs. 1.5 mg/kg p.o. for nifedipine.  
 IT 116796-71-5P 116796-72-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as calcium-antagonistic antihypertensive and vasodilator)  
 RN 116796-71-5 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 2-amino-5-[bis(2-propenyloxy)phosphinyl]-1,4-dihydro-6-methyl-4-(2-nitrophenyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 116796-72-6 CAPLUS  
 CN 3-Pyridinecarboxylic acid, 2-amino-5-[bis(2-propenyloxy)phosphinyl]-1,4-dihydro-6-methyl-4-[2-(trifluoromethyl)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1988:466891 CAPLUS  
 DOCUMENT NUMBER: 109:66891  
 TITLE: Preparation of 2-substituted 1,4-dihydropyridine derivatives as antihypertensives  
 INVENTOR(S): Kimura, Kiyoshi; Kise, Masahiro; Morita, Iwao; Tomita, Toshio; Tsuda, Masami  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: Ger. Offen., 10 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3736687	A1	19880511	DE 1987-3736687	19871029
JP 63115890	A	19880520	JP 1986-261587	19861031
GB 2196631	A	19880505	GB 1987-24868	19871023
GB 2196631	B	19900711		
FR 2606019	A1	19880506	FR 1987-14928	19871028
FR 2606019	B1	19910531		
US 4857515	A	19890815	US 1987-115170	19871030

PRIORITY APPLN. INFO.: CASREACT 109:66891; MARPAT 109:66891  
 OTHER SOURCE(S): GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R1 = alkenyl, alkyl; or R1R1 = (CH2)3; R2 = NO2, CF3, halo; R3 = lower alkyl; R4 = (MeO)2CH, HCO, HOCH2, CN] are prepared as Ca2+ antagonists, hypotensives, and vasodilators for treatment and prophylaxis of circulatory diseases. Me 3-amino-4-dimethoxycrotonate underwent cyclocondensation with 2-[1-(2-nitrobenzylidene)acetyl] -2-oxo-1,3,2-dioxaphorrorinan in refluxing MeCN to form I [R1R1 = (CH2)3, R2 = 2-NO2, R3 = Me, R4 = (MeO)2CH, which was hydrolyzed with HCl in Me2CO to the 2-formyl derivative and then converted via the oxime to the 2-cyano derivative

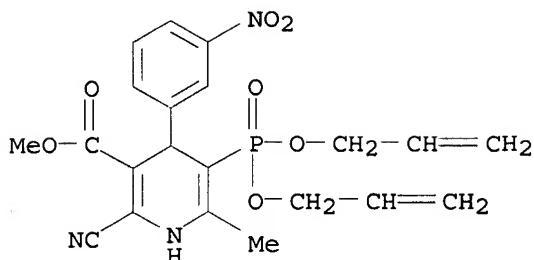
(II). II at 1.6 mg/kg orally decreased the blood pressure in spontaneously hypertensive rats by 30%.

IT 115550-24-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrolysis of, in antihypertensive preparation)

RN 115550-24-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(2-propenyl)phosphoryl]-2-(dimethoxymethyl)-1,4-dihydro-6-methyl-4-(3-nitrophenyl)-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:167687 CAPLUS

DOCUMENT NUMBER: 108:167687

TITLE: Preparation of dihydropyridine-5-phosphonamidic acid derivatives for treatment of circulation disorders

INVENTOR(S): Kamikawaiji, Masumasa; Seto, Kyotomo; Sakota, Ryozo; Tanaka, Sakuya

PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

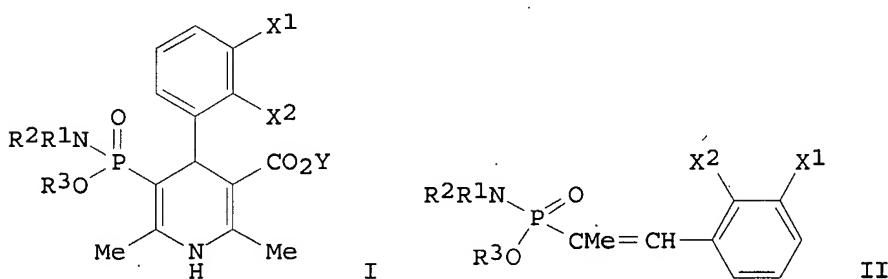
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62195392	A	19870828	JP 1986-36402	19860220
JP 06015553	B	19940302		
PRIORITY APPLN. INFO.:			JP 1986-36402	19860220
GI				



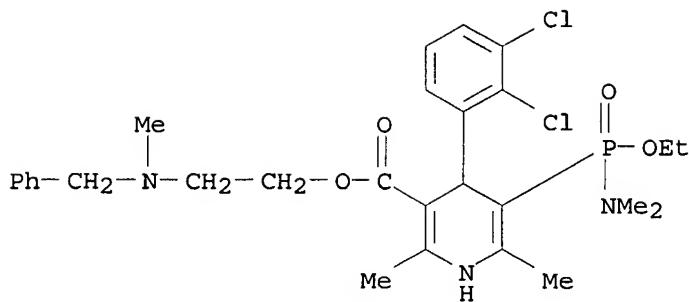
AB The title compds. [I; R<sub>1</sub>, R<sub>2</sub> = H, C<sub>1</sub>-6 alkyl, R<sub>1</sub>R<sub>2</sub> = alkyl-substituted 1,4-butylene; R<sub>3</sub> = C<sub>1</sub>-10 alkyl, R<sub>2</sub>R<sub>3</sub> = alkyl substituted (CH<sub>2</sub>)<sub>2</sub>-3; X<sub>1</sub>, X<sub>2</sub> = H, NO<sub>2</sub>, CF<sub>3</sub>, alkyl, (halo)alkyl, F, Cl; Y = C<sub>1</sub>-4 alkyl, diphenyl- or dialkylaminoethyl, etc.] are prepared Refluxing a solution of styrene derivative

II [R<sub>1</sub> = R<sub>2</sub> = Me, R<sub>3</sub> = Et, X<sub>1</sub> = Cl, X<sub>2</sub> = H] and H<sub>2</sub>NCMe:CHCO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>2</sub>Ph)Me in MePh gave 81% I (R<sub>1</sub> = R<sub>2</sub> = Me, R<sub>3</sub> = Et, X<sub>1</sub> = H, X<sub>2</sub> = Cl, Y = CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>2</sub>Ph)Me], which was converted to its HCl salt (III) to show pID50 of 7.4 as Ca antagonist and ED<sub>30</sub> of 0.26 as hypotensive. A capsule formula was prepared from III 5, corn starch 145, microcryst. cellulose 145, and Mg stearate 5 g (for 1000 capsules).

IT 113954-80-6P 113954-81-7P 113954-82-8P

113954-83-9P 113954-84-0P 113954-85-1P

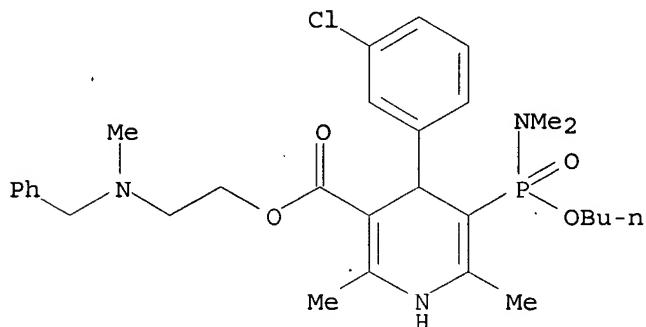
113954-86-2P 113954-87-3P 113954-88-4P



RN 113979-08-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[butoxy(dimethylamino)phosphinyl]-4-(3-chlorophenyl)-1,4-dihydro-2,6-dimethyl-, 2-[methyl(phenylmethyl)amino]ethyl ester, (-) (CA INDEX NAME)

Rotation (-).



L4 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:31312 CAPLUS

DOCUMENT NUMBER: 108:31312

TITLE: Synthesis and antihypertensive activities of

1,4-dihydropyridine-5-phosphonate derivatives. I

AUTHOR(S): Morita, Iwao; Tada, Shinichi; Kunimoto, Katsutoshi; Tsuda, Masami; Kise, Masahiro; Kimura, Kiyoshi

CORPORATE SOURCE: Res. Lab., Nippon Shinyaku Co., Ltd., Kyoto, 601, Japan

SOURCE: Chemical &amp; Pharmaceutical Bulletin (1987), 35(9), 3898-904

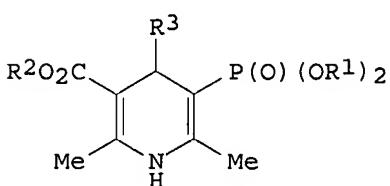
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

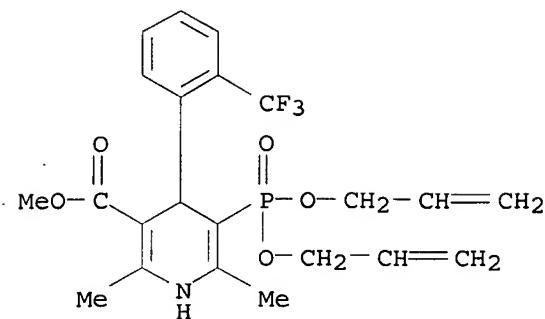
LANGUAGE: English

OTHER SOURCE(S): CASREACT 108:31312

GI



I



L4 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:214127 CAPLUS

DOCUMENT NUMBER: 106:214127

TITLE: Phosphonopyridines and their 1,4-dihydro derivatives  
as calcium antagonists, and a process for their  
preparationINVENTOR(S): Gandolfi, Carmelo A.; Frigerio, Marco; Spinelli,  
Silvano; Riva, Carlo; Tofanetti, Odoardo; Tognella,  
Sergio

PATENT ASSIGNEE(S): Boehringer Biochemia Robin S.p.A., Italy

SOURCE: Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

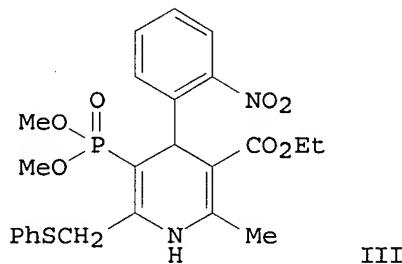
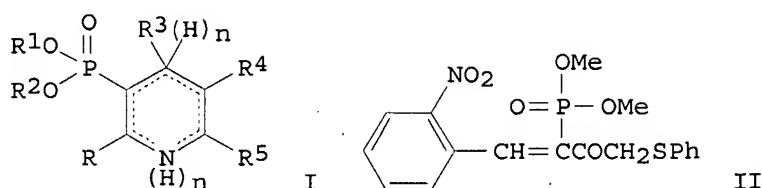
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 210571	A1	19870204	EP 1986-110013	19860721
EP 210571	B1	19900530		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE AT 53216	T	19900615	AT 1986-110013 IT 1985-21818 EP 1986-110013	19860721 A 19850801 A 19860721
PRIORITY APPLN. INFO.:				
OTHER SOURCE(S):	MARPAT 106:214127			
GI				



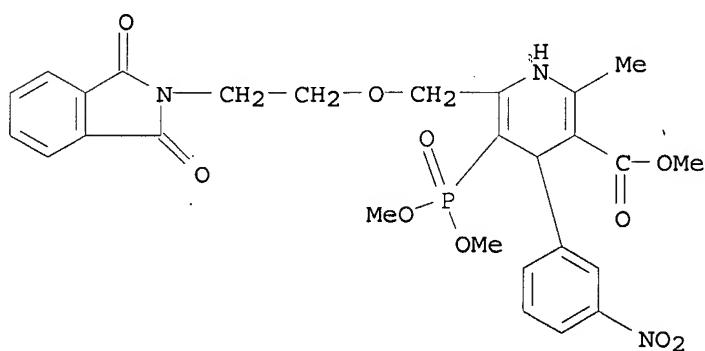
AB Title compds. I [ $n = 0$  (aromatic ring), 1 (1,4-dihydropyridine ring); R = (un)substituted alkyl; R<sub>1</sub>, R<sub>2</sub> = H, alkyl, Ph, PhCH<sub>2</sub>; R<sub>3</sub> = bicyclic ring (e.g., naphthyl,  $\alpha$ -benzofuroxanyl), heterocyclyl, (un)substituted Ph; R<sub>4</sub> = Ac, Bz, cyano, NO<sub>2</sub>, (un)substituted CONH<sub>2</sub>, CO<sub>2</sub>H, Ph; R<sub>5</sub> = alkyl, Ph, PhCH<sub>2</sub>; R  $\neq$  alkyl when  $n = 1$  and R<sub>4</sub> = carboxy ester group] are prepared as Ca antagonists (no data). A mixture of phosphonate (Z/E)-II (preparation given), Me(H<sub>2</sub>N)C:CHCO<sub>2</sub>Et, and HCl catalyst in EtOH was refluxed for 3 h under N to give (nitrophenyl)dihydropyridinephosphonate III.

IT 107347-12-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrazinolysis of)

preparation and  
BN 107347-13-6 CARLIUS

RN 107347-12-6 CAPLUS  
CN 3-Pyridinecarboxylic acid, 6-[[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethoxy]methyl]-5-(dimethoxyphosphinyl)-1,4-dihydro-2-methyl-4-(3-nitrophenyl)- methyl ester (CA INDEX NAME)

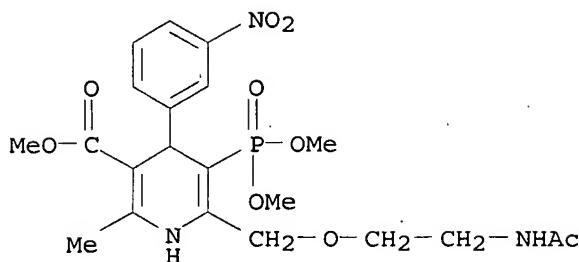


IT 95242-45-8P 98399-25-8P 98399-27-0P  
102065-36-1P 107347-08-0P 107347-10-4P

107347-13-7P 107347-14-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of as calcium antagonist)

BN 95243-45-8 CARLIUS (preparation of)

RN 93242-45-6 CAPLOS  
CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



L4 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:102546 CAPLUS

DOCUMENT NUMBER: 106:102546

TITLE: Dihydropyridine-5-phosphonic acid diamide derivatives

INVENTOR(S): Kamikawaiji, Masuaki; Seto, Kiyotomo; Sakota, Ryozo; Tanaka, Sakuya

PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

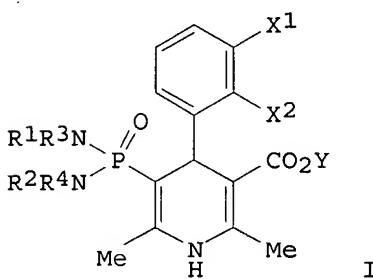
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

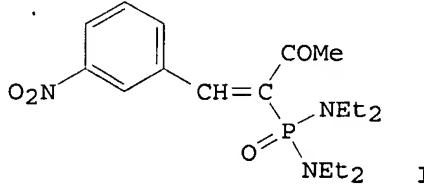
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61210092	A	19860918	JP 1985-50796	19850314
JP 04053870	B	19920827		
PRIORITY APPLN. INFO.:			JP 1985-50796	19850314
GI				



I



II

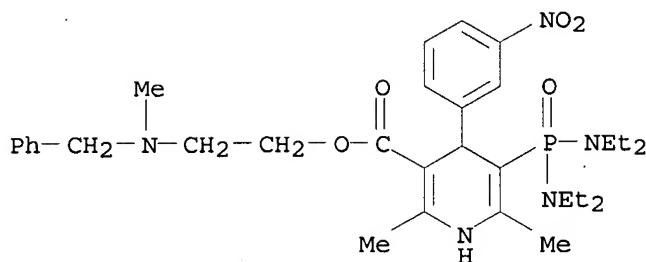
AB The title compds. I (R1, R2 = C1-4 alkyl; R3, R4 = C1-4 alkyl, R3R4 = alkylene; X1, X2 = H, NO<sub>2</sub>, halo, CF<sub>3</sub>; Y = C1-4 alkyl, PhCH<sub>2</sub>NMeCH<sub>2</sub>CH<sub>2</sub>, etc.), effective vasodilators for treating hypertension, etc., at 0.001-100 mg/kg orally, are prepared. Thus, refluxing a mixture of 1.1 g II and 0.9 g H<sub>2</sub>NMe:CHCO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NMeCH<sub>2</sub>Ph in MePh to give 37% I (R1-4 = Et, X1 = NO<sub>2</sub>, X2 = H, Y = PhCH<sub>2</sub>NMeCH<sub>2</sub>CH<sub>2</sub>), which (1.0 g as HCl salt) was mixed, in a powder formulation, with lactose 88.0, microcryst. cellulose 10.0, and methylcellulose 1.0 g.

IT 106937-00-2P 106937-01-3P 106937-02-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as vasodilator)

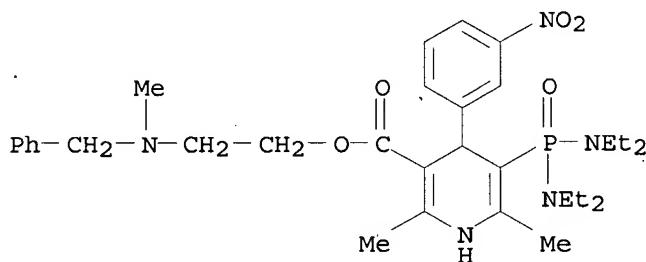
RN 106937-00-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(diethylamino)phosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



RN 106937-01-3 CAPLUS

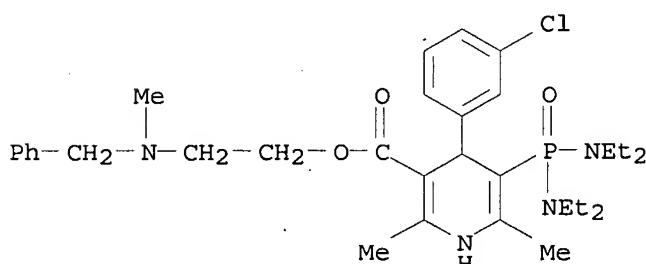
CN 3-Pyridinecarboxylic acid, 5-[bis(diethylamino)phosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

RN 106937-02-4 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(diethylamino)phosphinyl]-4-(3-chlorophenyl)-1,4-dihydro-2,6-dimethyl-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



L4 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:534148 CAPLUS

DOCUMENT NUMBER: 105:134148

ORIGINAL REFERENCE NO.: 105:21657a, 21660a

TITLE: Pyridylphosphonates

INVENTOR(S): Kimura, Kiyoshi; Morita, Iwao

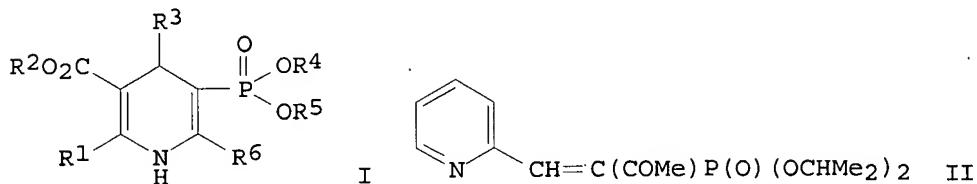
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.

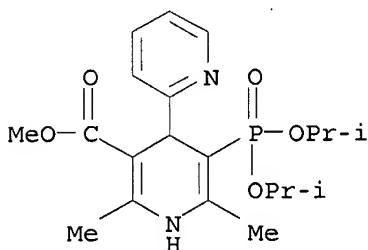
CODEN: JKXXAF

DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61063689	A	19860401	JP 1984-184936	19840903
PRIORITY APPLN. INFO.:			JP 1984-184936	19840903
OTHER SOURCE(S):	CASREACT 105:134148			
GI				



AB The title compds. (I; R1 = alkyl; R2 = H, saturated or unsatd. hydrocarbon residue; R3 = heterocyclic; R4, R5 = H, alkyl, alkenyl, R4R5 = ring-forming radical; R6 = alkyl), effective vasodilators at 10-5 g in vitro and hypotensives at 30 mg/kg orally in rats, are prepared. Thus, refluxing 2.5 g II and 0.92 g Me 3-aminocrotonate in Me<sub>2</sub>CHOH gave 1.96 g I (R1 = R2 = R6 = Me, R3 = 2-pyridyl, R4 = R5 = Me<sub>2</sub>CH).  
 IT 104245-96-7P 104245-97-8P 104245-98-9P  
 104245-99-0P 104246-00-6P 104246-01-7P  
 104246-02-8P 104246-03-9P 104246-04-0P  
 104246-05-1P 104246-06-2P 104246-07-3P  
 104246-09-5P 104246-10-8P 104246-11-9P  
 104246-13-1P 104246-14-2P 104246-16-4P  
 104270-30-6P 104270-31-7P 104270-32-8P  
 104270-33-9P 104270-34-0P  
 RN RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as vasodilator and hypotensive)  
 RN 104245-96-7 CAPLUS  
 CN [2,4'-Bipyridine]-3'-carboxylic acid, 5'-[bis(1-methylethoxy)phosphinyl]-  
 1',4'-dihydro-2',6'-dimethyl-, methyl ester (CA INDEX NAME)



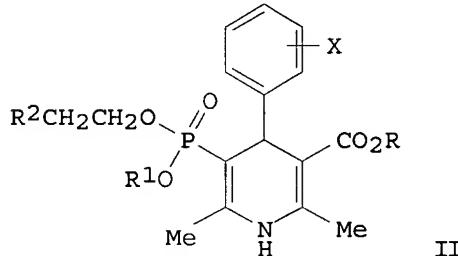
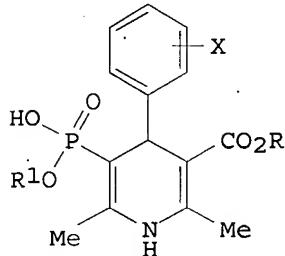
RN 104245-97-8 CAPLUS  
CN [2,4'-Bipyridine]-3'-carboxylic acid, 5'-[bis(1-methylethoxy)phosphinyl]-1',4'-dihydro-2',6'-dimethyl-, 2-[methyl(phenylmethyl)amino]ethyl ester  
(CA INDEX NAME)

L4 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1986:479162 CAPLUS  
DOCUMENT NUMBER: 105:79162  
ORIGINAL REFERENCE NO.: 105:12853a,12856a  
TITLE: Dihydropyridine-5-phosphonic acid monoesters  
INVENTOR(S): Seto, Kiyotomo; Tanaka, Sakuya; Sakota, Ryozo  
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61027995	A	19860207	JP 1984-148979	19840718
JP 04060477	B	19920928		
PRIORITY APPLN. INFO.:			JP 1984-148979	19840718
CT				

PRIORITY APPLN. INFO.:

GI

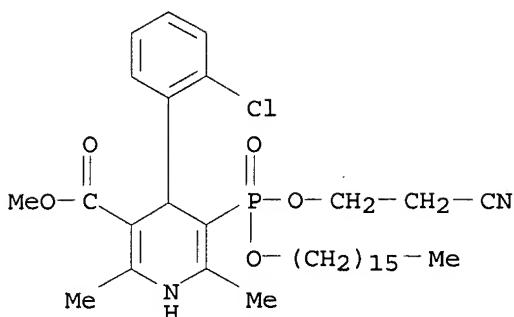


AB The title esters (I; R = C1-6 alkyl, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, etc.; R<sub>1</sub> = C1-16 alkyl; X = H, NO<sub>2</sub>, CF<sub>3</sub>, halo), effective antihypertensives at 1.4 mg/kg in rats and Ca antagonists at 2.5 + 10<sup>-6</sup> M in guinea pigs, were prepared by base-catalyzed hydrolysis of II (R<sub>2</sub> = cyano, NO<sub>2</sub>, halo). Thus, an aqueous solution of NaOH was added to a solution of 3.5 g II (R = R<sub>1</sub> = Me, R<sub>2</sub> = cyano, X = 2-Cl) in EtOH at room temperature to give 90% I (R = R<sub>1</sub> = Me, X = 2-Cl). A capsule formulation consisted of I 5, corn starch 145, microcryst. cellulose 145, and Mg stearate 5 g (for 1000 capsules).

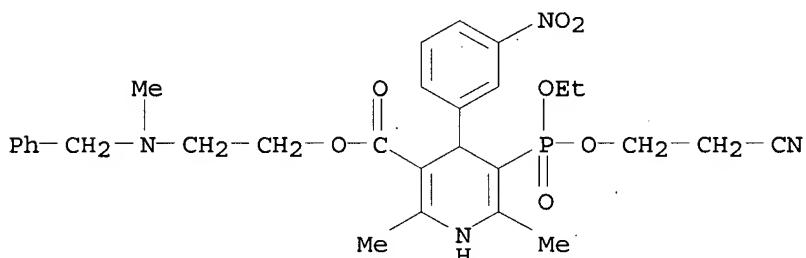
X 103763-89-9 103763-90-2 103763-91-3  
IT 103763-92-4 103763-93-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydrolysis of)

RN 103763-89-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 4-(2-chlorophenyl)-5-[(2-cyanoethoxy)methoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-, methyl ester (CA INDEX NAME)



RN 103763-93-5 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[(2-cyanoethoxy)ethoxyphosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester  
(CA INDEX NAME)

L4 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:443089 CAPLUS

DOCUMENT NUMBER: 105:43089

ORIGINAL REFERENCE NO.: 105:7145a,7148a

TITLE: Dihydropyridine-2-amino-5-phosphate derivatives

INVENTOR(S): Seto, Kiyotomo; Tanaka, Sakuya; Sakota, Ryozo

PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

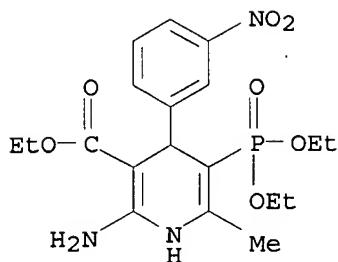
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

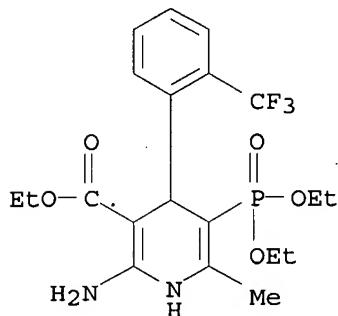
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61037793	A	19860222	JP 1984-159178	19840731
JP 04047678	B	19920804		
PRIORITY APPLN. INFO.:			JP 1984-159178	19840731
OTHER SOURCE(S):	CASREACT	105:43089		
GI				



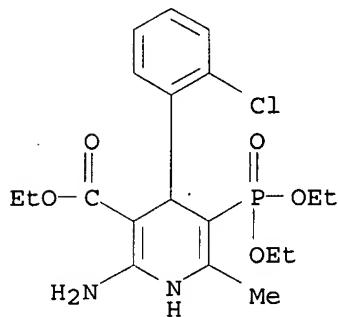
RN 102994-35-4 CAPLUS

CN 3-Pyridinecarboxylic acid, 2-amino-5-(diethoxyphosphinyl)-1,4-dihydro-6-methyl-4-[2-(trifluoromethyl)phenyl]-, ethyl ester (CA INDEX NAME)



RN 102994-36-5 CAPLUS

CN 3-Pyridinecarboxylic acid, 2-amino-4-(2-chlorophenyl)-5-(diethoxyphosphinyl)-1,4-dihydro-6-methyl-, ethyl ester (CA INDEX NAME)



L4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:207457 CAPLUS

DOCUMENT NUMBER: 104:207457

ORIGINAL REFERENCE NO.: 104:32893a, 32896a

TITLE: Dihydropyridine derivatives

INVENTOR(S): Tsuda, Yoshiaki

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Factory, Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

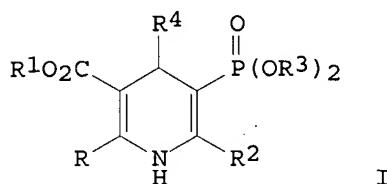
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60258194	A	19851220	JP 1984-113718	19840601
PRIORITY APPLN. INFO.:			JP 1984-113718	19840601
GI				

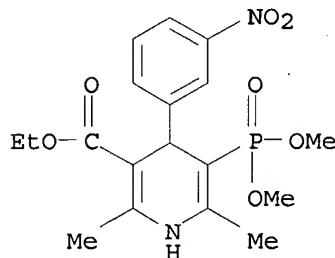


AB Dihydropyridinephosphonate derivs. I (R, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> = alkyl; R<sub>4</sub> = naphthyl, Ph mono-, di-, or trisubstituted by nitro, halo, haloalkyl, OH, or cyano), useful as vasodilators, were prepared. Thus, refluxing a mixture of 1.6 g m-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CHO, 1.3 g Me(H<sub>2</sub>N)C:CHCO<sub>2</sub>Et, 1.7 g MeCOCH<sub>2</sub>P(O)(OMe)<sub>2</sub>, and 10 mL Me<sub>2</sub>CHOH for 20 h gave I (R = R<sub>2</sub> = R<sub>3</sub> = Me, R<sub>1</sub> = Et, R<sub>4</sub> = 3-nitrophenyl).

IT 102065-36-1P 102065-37-2P 102065-38-3P  
 102065-39-4P 102065-40-7P 102065-41-8P  
 102065-42-9P 102065-43-0P 102065-44-1P  
 102065-45-2P 102065-46-3P 102065-47-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as vasodilator)

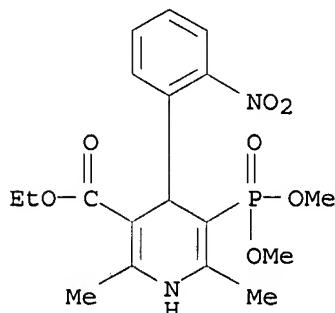
RN 102065-36-1 CAPPLUS

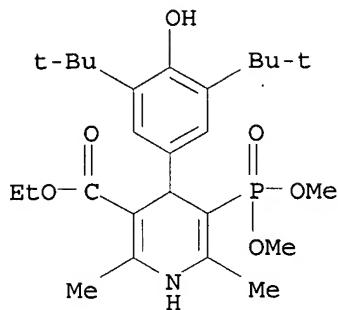
CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, ethyl ester (CA INDEX NAME)



RN 102065-37-2 CAPPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-, ethyl ester (CA INDEX NAME)





L4 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:578452 CAPLUS

DOCUMENT NUMBER: 103:178452

ORIGINAL REFERENCE NO.: 103:28727a,28730a

TITLE: 1,4-Dihydropyridine-5-phosphonic acid ester

INVENTOR(S): Seto, Kiyotomo; Tanaka, Sakuya; Sakoda, Ryozo

PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 34 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

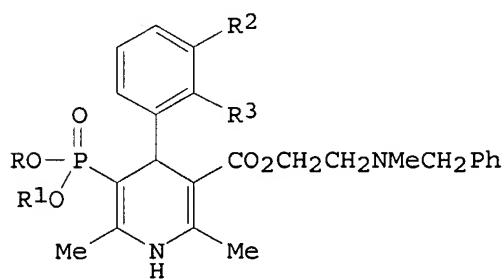
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 141221	A1	19850515	EP 1984-111185	19840919
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 60069089	A	19850419	JP 1983-177710	19830926
JP 03079359	B	19911218		
JP 61030591	A	19860212	JP 1984-151782	19840720
JP 04060478	B	19920928		
PRIORITY APPLN. INFO.:			JP 1983-177710	A 19830926
			JP 1984-151782	A 19840720

OTHER SOURCE(S): MARPAT 103:178452

GI

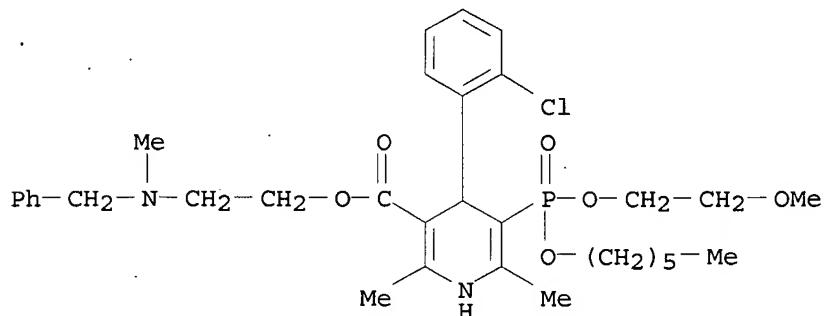


I

AB The antihypertensive and vasodilator title compds. I (R, R1 = CH2CH2OMe, C1-10 alkyl; R2 = H, Cl, NO2, CF3; R3 = H, Cl, CF3) were prepared. Thus, H2NCMe:CHCO2CH2CH2NMeCH2Ph underwent cyclocondensation with (EtO)2P(O)C(COMe):CHC6H4CF3-3, to give I (R = R1 = Et; R2 = CF3, R3 = H) (II). II was antihypertensive, with an ED30 of 0.13 mg/kg in spontaneously hypertensive rats. II was also a calcium antagonist in vitro.

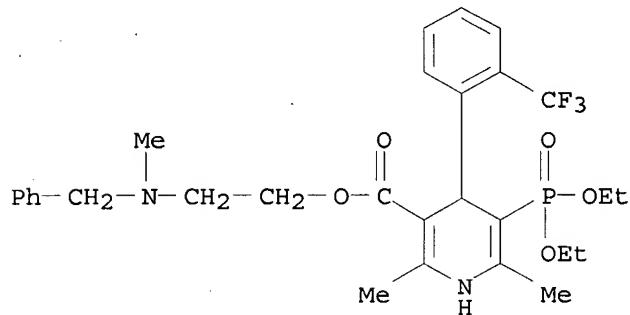
10/549, 510

CN 3-Pyridinecarboxylic acid, 4-(2-chlorophenyl)-5-[(hexyloxy)(2-methoxyethoxy)phosphinyl]-1,4-dihydro-2,6-dimethyl-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



RN 98907-65-4 CAPLUS

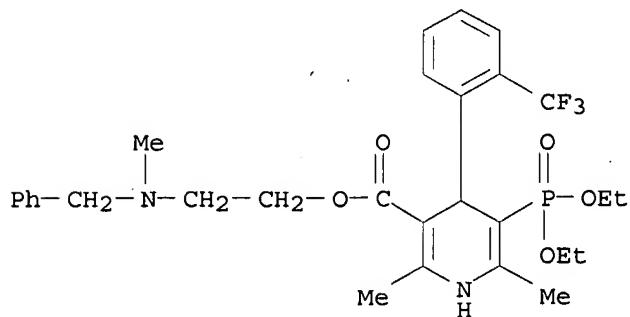
3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[2-(trifluoromethyl)phenyl]-, 2-[methyl(phenylmethyl)amino]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 98907-66-5 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-[2-(trifluoromethyl)phenyl]-, 2-[methyl(phenylmethyl)amino]ethyl ester  
(CA INDEX NAME)

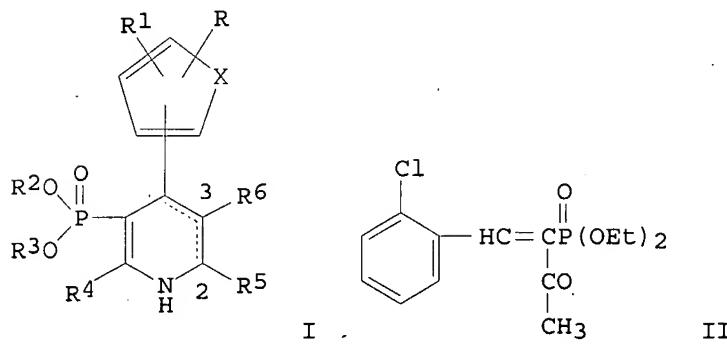


ACCESSION NUMBER: 1985:542188 CAPLUS  
DOCUMENT NUMBER: 103:142188  
ORIGINAL REFERENCE NO.: 103:22779a, 22782a  
TITLE: Dihydropyridine-5-phosphonate derivatives  
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.

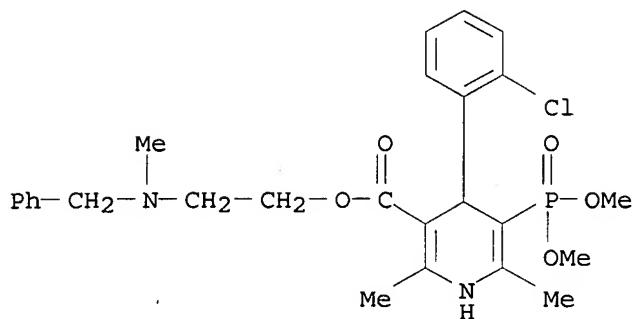
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60069089	A	19850419	JP 1983-177710	19830926
JP 03079359	B	19911218		
EP 141221	A1	19850515	EP 1984-111185	19840919
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
EP 141222	A1	19850515	EP 1984-111187	19840919
EP 141222	B1	19890412		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 42105	T	19890415	AT 1984-111187	19840919
CA 1339372	C	19970826	CA 1984-463611	19840919
US 4576934	A	19860318	US 1984-654473	19840926
US 4839361	A	19890613	US 1985-792981	19851030
PRIORITY APPLN. INFO.:				
			JP 1983-177710	A 19830926
			JP 1984-151782	A 19840720
			JP 1984-163649	A 19840803
			EP 1984-111187	A 19840919
			US 1984-654473	A2 19840926

GI



AB The title phosphonates I (R, R1 = H, O2N, CF3, halo, HO, cyano, etc.; R2, R3 = alkyl, alkenyl, aryl, aralkyl, etc.; R4, R5 = aryl, styryl; X = O, S, CH:CH, CH:N; R6 = alkoxy carbonyl, etc.), effective Ca antagonists at 0.001-100 mg/kg orally, diuretics at 5-20 mg/kg, and hypotensives at 5-50 mg/kg, were prepared. Thus, a solution of 2.2 g II and 1.1 g Me 3-aminocrotonate in C6H6 was refluxed 38 h to give 55% I (2,3-unsatd., R = H, R1 = 2-Cl, R2 = R3 = Et, R4 = R5 = Me, R6 = MeO2C, X = CH:CH).

IT	98371-12-1P	98371-13-2P	98371-14-3P
	98371-15-4P	98371-16-5P	98371-17-6P
	98371-18-7P	98371-19-8P	98398-80-2P
	98398-81-3P	98398-82-4P	98398-83-5P
	98398-84-6P	98398-85-7P	98399-08-7P
	98399-09-8P	98399-10-1P	98399-11-2P



L4 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:132271 CAPLUS

DOCUMENT NUMBER: 102:132271

ORIGINAL REFERENCE NO.: 102:20767a,20770a

TITLE: Dihydropyridyl phosphate derivatives

PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 41 pp.

CODEN: JKXXAF

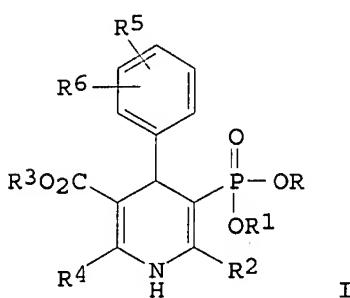
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59161392	A	19840912	JP 1983-36211	19830304
JP 03065351	B	19911011		
GB 2140015	A	19841121	GB 1984-4386	19840220
GB 2140015	B	19870729		
EP 121117	A1	19841010	EP 1984-102249	19840302
EP 121117	B1	19890830		
R: CH, DE, FR, IT, LI, NL, SE				
ES 530248	A1	19850516	ES 1984-530248	19840302
US 4535073	A	19850813	US 1984-585574	19840302
CA 1254206	A1	19890516	CA 1984-448718	19840302
ES 537717	A1	19860101	ES 1984-537717	19841116
PRIORITY APPLN. INFO.:			JP 1983-36211	A 19830304
OTHER SOURCE(S):			CASREACT 102:132271; MARPAT 102:132271	
GI				



AB The title phosphate derivs. I (R, R1 = H, hydrocarbons, tetrahydrofurfuryl; R2 = alkyl; R3 = alkoxy, aryloxy, aralkoxy, etc.; R4 = alkyl; R5, R6 = H, NO2, cyano, CF3, etc.) (apprx.180 compds.) were prepared

by, e.g., reaction of  $R_5R_6C_6H_3CH:C(COR_2)P(O)(OR_1)$  (II) with  $H_2NCR_4:CHCO_2R_3$  (III). I were coronary vasodilators and hypotensives, with  $LD_{50} > 400$  mg/kg (p.o.). Thus, a mixture of 1.85 g II ( $R = R_2 = Me$ ,  $R_5 = 3-NO_2$ ,  $R_6 = H$ ) and 0.75 g III ( $R_3 = R_4 = Me$ ) in  $Me_2CHOH$  was refluxed 4 h to give 42% I ( $R = R_4 = Me$ ,  $R_5 = 3-NO_2$ ,  $R_6 = H$ ).

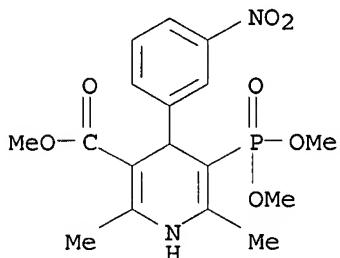
IT 95242-45-8P 95242-46-9P 95242-47-0P

95242-48-1P 95242-49-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

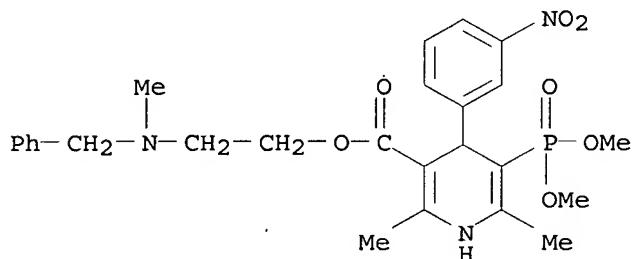
RN 95242-45-8 CAPPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



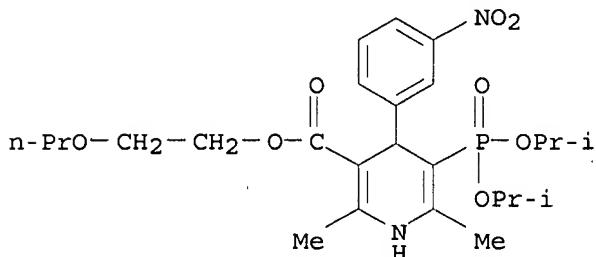
RN 95242-46-9 CAPPLUS

CN 3-Pyridinecarboxylic acid, 5-(dimethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester (CA INDEX NAME)



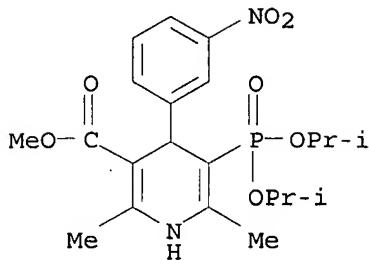
RN 95242-47-0 CAPPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(1-methylethoxy)phosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-propoxyethyl ester (CA INDEX NAME)

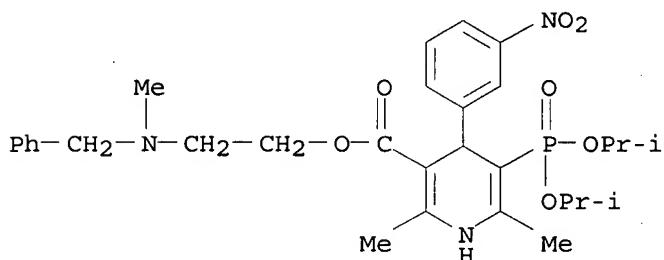


RN 95242-48-1 CAPPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(1-methylethoxy)phosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl ester (CA INDEX NAME)



RN 95242-49-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[bis(1-methylethoxy)phosphinyl]-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-[methyl(phenylmethyl)amino]ethyl ester  
(CA INDEX NAME)

L4 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1976:446818 CAPLUS

DOCUMENT NUMBER: 85:46818

ORIGINAL REFERENCE NO.: 85:7619a,7622a

TITLE: Contributions to the reaction behavior of  
oxoalkanephosphonic acid dialkyl esters

AUTHOR(S): Issleib, K.; Wolff, R.; Lengies, M.

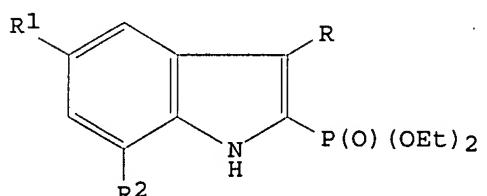
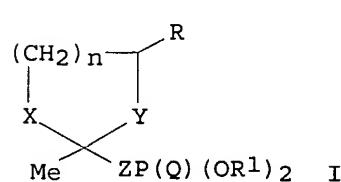
CORPORATE SOURCE: Sekt. Chem., Martin-Luther-Univ., Halle/Saale, Ger.  
Dem. Rep.SOURCE: Journal fuer Praktische Chemie (Leipzig) (1976),  
318(2), 207-20

CODEN: JPCEAO; ISSN: 0021-8383

DOCUMENT TYPE: Journal

LANGUAGE: German

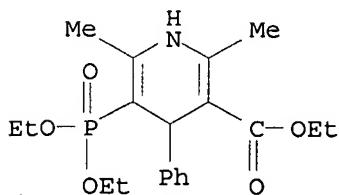
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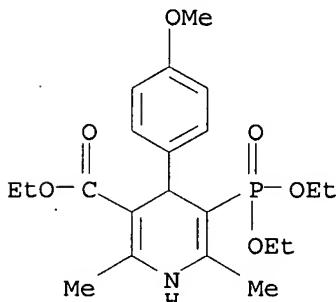
AB AcZP(Q)(OR1)2 cyclized with diols and thiidiols to give 8-26.3% 19 cyclic ketals and thioketals I (X, Y, Q = O, S; Z = CH2, CH2CHPh; n = 1, 2; R = H, Me, CH2Cl; R1 = Et, Bu). The condensation of benzenediazonium chlorides 2,4-R2R1C6H3N2+Cl- with RCH2CHAcP(O)(OEt)2 gave arylhydrazones, 2,4-R2R1C6H3NHN:C(CH2R)P(O)(OEt)2, which cyclized to give 2.4-23.1% 12 indolephosphonates II (R = Ph, p-tolyl, p-anisyl, p-ClC6H4, Me; R1 = H, MeO, O2N, Me, Cl, CO2Me, NH2; R2 = H, Cl).

10/549,510

IT 59823-27-7P 59823-28-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 59823-27-7 CAPLUS  
CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-2,6-dimethyl-4-phenyl-, ethyl ester (CA INDEX NAME)



RN 59823-28-8 CAPLUS  
CN 3-Pyridinecarboxylic acid, 5-(diethoxyphosphinyl)-1,4-dihydro-4-(4-methoxyphenyl)-2,6-dimethyl-, ethyl ester (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 10:29:49 ON 18 JAN 2008)

FILE 'REGISTRY' ENTERED AT 10:30:06 ON 18 JAN 2008

L1 STRUCTURE UPLOADED  
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L3 278 S L1 FULL

FILE 'CAPLUS' ENTERED AT 10:30:41 ON 18 JAN 2008

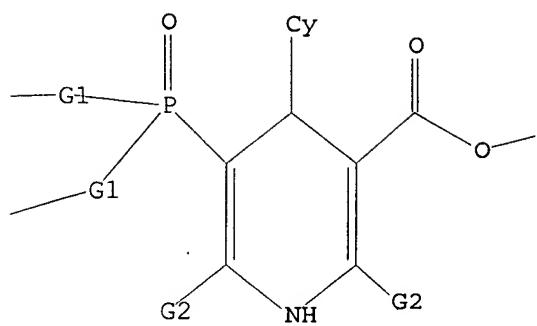
L4 26 S L3

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L1 HAS NO ANSWERS

L1 STR

10/549,510



G1 O, N

G2 C, N, CN

Structure attributes must be viewed using STN Express query preparation.

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